

AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application.

Listing of Claims:

1. (Currently Amended) An osteoinductive powder comprising:

(a) demineralized bone matrix (DBM) particles in an amount in the range of about 40 to about 70 wt%, and

(b) a calcium phosphate powder in an amount in the range of about 25 to about 60 wt%,

wherein said osteoinductive powder forms a formable, self-hardening, poorly crystalline apatitic (PCA) calcium phosphate paste when admixed with a physiologically acceptable liquid, and wherein said paste is capable of hardening to form a PCA calcium phosphate having a compressive strength of greater than at least about 1 MPa.

2. (Cancelled)

3. (Currently Amended) The osteoinductive powder of claim 1, wherein said DBM particles comprise ~~are present in an amount less than~~ about 60 wt% of said osteoinductive powder.

4. (Currently Amended) The osteoinductive powder of claim 3, wherein said DBM particles comprise ~~are present in an amount less than~~ about 50 wt% of said osteoinductive powder.

5-6 (Cancelled)

7. (Original) The osteoinductive powder of claim 1, wherein said DBM particles have a

particle size of less than about 850 μm .

8. (Original) The osteoinductive powder of claim 1, wherein said DBM particles have a particle size in the range of about 125 to about 850 μm .

9. (Currently Amended) The osteoinductive powder of claim 1 ~~7~~, wherein said DBM particles have a particle size in the range of about 53 to about 125 μm .

10. (Currently Amended) The osteoinductive powder of claim 1 ~~7~~, wherein said DBM particles have a particle size of less than about 125 μm .

11. (Original) The osteoinductive powder of claim 1, wherein said calcium phosphate powder comprises amorphous calcium phosphate and a second calcium phosphate.

12. (Original) The osteoinductive powder of claim 11, wherein said second calcium phosphate is an acidic or a neutral calcium phosphate.

13. (Original) The osteoinductive powder of claim 12, wherein said acidic calcium phosphate is calcium metaphosphate, dicalcium phosphate dihydrate, heptacalcium phosphate, tricalcium phosphate, calcium pyrophosphate dihydrate, poorly crystalline hydroxyapatite, calcium pyrophosphate, or octacalcium phosphate.

14. (Original) The osteoinductive powder of claim 13, wherein said acidic calcium phosphate is dicalcium phosphate dihydrate (DCPD).

15. (Original) The osteoinductive powder of claim 11, wherein said amorphous calcium phosphate and said second calcium phosphate have an average crystalline domain size of less than about 100 nm.

16. (Original) The osteoinductive powder of claim 1, wherein said calcium phosphate powder is subjected to a high energy milling process prior to admixing with said DBM particles.

17. (Original) The osteoinductive powder of claim 1 further comprising at least one supplemental material selected from a cohesiveness agent, a biologically active agent, and an effervescent agent.

18. (Currently Amended) The osteoinductive powder of claim 17, wherein said cohesiveness agent comprises ~~is present in an amount in the range of~~ about 0.5 + to about 20 wt% of said osteoinductive powder.

19. (Currently Amended) The osteoinductive powder of claim 17, wherein said cohesiveness agent comprises ~~is present in an amount of~~ less than about 20 wt% of said osteoinductive powder.

20. (Currently Amended) The osteoinductive powder of claim 19, wherein said cohesiveness agent comprises ~~is present in an amount of~~ less than about 10 wt% of said osteoinductive powder.

21. (Currently Amended) The osteoinductive powder of claim 20, wherein said cohesiveness agent comprises ~~is present in an amount of~~ less than about 5 wt% of said osteoinductive powder.

22. (Currently Amended) The osteoinductive powder of claim 21, wherein said cohesiveness agent comprises ~~is present in an amount of~~ less than about 1 wt% of said osteoinductive powder.

23. (Currently Amended) The osteoinductive powder of claim 17, wherein said cohesiveness agent ~~is comprises~~ a polymer selected from polysaccharides, nucleic acids, carbohydrates, proteins, polypeptides, poly(α -hydroxy acids), poly(lactones), poly(amino acids), poly(anhydrides), poly(orthoesters), poly(anhydride-co-imides), poly(orthocarbonates), poly(α -hydroxy alkanoates), poly(dioxanones), poly(phosphoesters), poly(L-lactide) (PLLA), poly(D,L-lactide) (PDLA), polyglycolide (PGA), poly(lactide-co-glycolide (PLGA), poly(L-lactide-co-D, L-lactide), poly(D,L-lactide-co-trimethylene carbonate), polyhydroxybutyrate (PHB), poly(ϵ -caprolactone), poly(δ -valerolactone), poly(γ -butyrolactone), poly(caprolactone), polyacrylic acid, polycarboxylic acid, poly(allylamine hydrochloride), poly(diallyldimethylammonium chloride), poly(ethyleneimine), polypropylene fumarate, polyvinyl alcohol, polyvinylpyrrolidone, polyethylene, polymethylmethacrylate, carbon fibers, poly(ethylene glycol), poly(ethylene oxide), poly(vinyl alcohol), poly(vinylpyrrolidone), poly(ethyloxazoline), poly(ethylene oxide)-co-poly(propylene oxide) block copolymers, poly(ethylene terephthalate)polyamide, and copolymers thereof.

24. (Original) The osteoinductive powder of claim 17, wherein said cohesiveness agent is selected from alginic acid, arabic gum, guar gum, xanthan gum, gelatin, chitin, chitosan, chitosan acetate, chitosan lactate, chondroitin sulfate, N,O-carboxymethyl chitosan, a dextran, fibrin glue, glycerol, hyaluronic acid, sodium hyaluronate, a cellulose, a glucosamine, a proteoglycan, a starch, lactic acid, a pluronic, sodium glycerophosphate, collagen, glycogen, a keratin, silk, and mixtures thereof.

25. (Original) The osteoinductive powder of claim 24, wherein said cellulose is

methylcellulose, carboxy methylcellulose, hydroxypropyl methylcellulose, or hydroxyethyl cellulose.

26. (Original) The osteoinductive powder of claim 24, wherein said dextran is α -cyclodextrin, β -cyclodextrin, γ -cyclodextrin, or sodium dextran sulfate.

27. (Original) The osteoinductive powder of claim 24, wherein said starch is hydroxyethyl starch or starch soluble.

28. (Original) The osteoinductive powder of claim 17, wherein said biologically active agent is selected from an antibody, an antibiotic, a polynucleotide, a polypeptide, a protein, an anti-cancer agent, a growth factor, and a vaccine.

29. (Original) The osteoinductive powder of claim 28, wherein said protein is an osteogenic protein.

30. (Original) The osteoinductive powder of claim 29, wherein said osteogenic protein is selected from BMP-2, BMP-4, BMP-5, BMP-6, BMP-7, BMP-10, BMP-12, BMP-13, and BMP-14.

31. (Currently Amended) The osteoinductive powder of claim 28, wherein said anti-cancer agent is selected from alkylating agents, platinum agents, antimetabolites, topoisomerase inhibitors, antitumor antibiotics, antimitotic agents, aromatase inhibitors, thymidylate synthase inhibitors, DNA antagonists, farnesyltransferase inhibitors, pump inhibitors, histone acetyltransferase inhibitors, metalloproteinase inhibitors, ribonucleoside reductase inhibitors, tumor necrosis factor (TNF) TNF alpha agonists, tumor necrosis factor (TNF) TNF alpha antagonists, endothelin A receptor antagonists, retinoic acid receptor agonists, immuno-

modulators, hormonal agents, antihormonal agents, photodynamic agents, and tyrosine kinase inhibitors.

32. (Currently Amended) The osteoinductive powder of claim 17, wherein said effervescent agent is sodium bicarbonate, carbon dioxide, air, nitrogen, helium, oxygen, or ~~and~~ argon.

33. (Currently Amended) The osteoinductive powder of claim 32, wherein said effervescent agent comprises ~~is present in an amount in the range of~~ about 1 to about 40 wt% of said osteoinductive powder.

34. (Currently Amended) The osteoinductive powder of claim 1, wherein said ~~osteoinductive powder forms a self-setting PCA calcium phosphate paste when admixed with said physiologically acceptable liquid, wherein said~~ paste hardens to form a PCA calcium phosphate having an overall Ca/P ratio of less than about 1.67.

35. (Currently Amended) The osteoinductive powder of claim 34, wherein said ~~osteoinductive powder forms a self-setting PCA calcium phosphate paste when admixed with said physiologically acceptable liquid, wherein said~~ paste hardens to form a PCA calcium phosphate having an overall Ca/P ratio of less than about 1.5 when admixed with said physiologically acceptable liquid.

36. (Currently Amended) The osteoinductive powder of claim 1, wherein said ~~osteoinductive powder forms a self-setting PCA calcium phosphate paste when admixed with said physiologically acceptable liquid, wherein said~~ paste hardens to form a PCA calcium phosphate having an overall Ca/P ratio in the range of about 1.0 to about 1.67 when admixed with said physiologically acceptable liquid.

37. (Currently Amended) An osteoinductive powder comprising:

(a) demineralized bone matrix (DBM) particles in an amount in the range of about 40 to about 70 wt%;

(b) a calcium phosphate powder in an amount in the range of about 25 to about 60 wt%;
and

(c) a biocompatible cohesiveness agent in an amount in the range of about 0.5 to 20 wt%;

wherein said osteoinductive powder forms a formable, self-hardening, poorly crystalline apatitic (PCA) calcium phosphate paste when admixed with a physiologically acceptable liquid, and wherein said paste is capable of hardening to form a PCA calcium phosphate having a compressive strength of greater than at least about 1 MPa.

38. (Withdrawn – Currently Amended) A formable, self-hardening, poorly crystalline apatitic (PCA) calcium phosphate paste suitable for use as a bone implant material comprising:

(a) a powder component comprising:

(i) demineralized bone matrix (DBM) particles in an amount in the range of about 40 to about 70 wt, and

(ii) a calcium phosphate powder in an amount in the range of about 25 to about 60 wt%; and

(b) a physiologically-acceptable fluid in an amount to produce a cohesive, formable paste, wherein said paste retains its cohesiveness when introduced at an implant site *in vivo* and hardens to form a PCA calcium phosphate having a compressive strength of greater than at least about 1 MPa.

39. (Cancelled)

40. (Withdrawn – Currently Amended) The paste of claim 38, wherein said DBM particles ~~comprise are present in an amount less than~~ about 60 wt% of said powder component.

41. (Withdrawn – Currently Amended) The paste of claim 40, wherein said DBM particles ~~comprise are present in an amount less than~~ about 50 wt% of said powder component.

42-43 (Cancelled)

44. (Withdrawn) The paste of claim 38, wherein said DBM particles have a particle size of less than about 850 μm .

45. (Withdrawn) The paste of claim 38, wherein said DBM particles have a particle size in the range of about 125 to about 850 μm .

46. (Withdrawn) The paste of claim 38, wherein said DBM particles have a particle size in the range of about 53 to about 125 μm .

47. (Withdrawn – Currently Amended) The paste of claim ~~38~~ 44, wherein said DBM particles have a particle size of less than about 125 μm .

48. (Withdrawn) The paste of claim 38, wherein said calcium phosphate powder comprises amorphous calcium phosphate and a second calcium phosphate.

49. (Withdrawn) The paste of claim 48, wherein said second calcium phosphate is an acidic or a neutral calcium phosphate.

50. (Withdrawn) The paste of claim 51, wherein said acidic calcium phosphate is calcium metaphosphate, dicalcium phosphate dihydrate, heptacalcium phosphate, tricalcium phosphate, calcium pyrophosphate dihydrate, poorly crystalline hydroxyapatite, calcium pyrophosphate, or octacalcium phosphate.

51. (Withdrawn) The paste of claim 50, wherein said acidic calcium phosphate is dicalcium phosphate dihydrate (DCPD).

52. (Withdrawn) The paste of claim 48, wherein said amorphous calcium phosphate and said second calcium phosphate have an average crystalline domain size of less than about 100 nm.

53. (Withdrawn) The paste of claim 38, wherein said calcium phosphate powder is subjected to a high energy milling process prior to admixing with said DBM particles.

54. (Withdrawn) The paste of claim 38 further comprising at least one supplemental material selected from a cohesiveness agent, a biologically active agent, and an effervescent agent.

55. (Withdrawn – Currently Amended) The paste of claim 54, wherein said cohesiveness agent comprises is present in an amount in the range of about 0.5 + to about 20 wt% of said powder component.

56. (Withdrawn – Currently Amended) The paste of claim 54, wherein said cohesiveness agent comprises is present in an amount of less than about 20 wt% of said powder

component.

57. (Withdrawn – Currently Amended) The paste of claim 56, wherein said cohesiveness agent comprises ~~is present in an amount of~~ less than about 10 wt% of said powder component.

58. (Withdrawn – Currently Amended) The paste of claim 57, wherein said cohesiveness agent comprises ~~is present in an amount of~~ less than about 5 wt% of said powder component.

59. (Withdrawn – Currently Amended) The paste of claim 58, wherein said cohesiveness agent comprises ~~is present in an amount of~~ less than about 1 wt% of said powder component.

60. (Withdrawn – Currently Amended) The paste of claim 54, wherein said cohesiveness agent ~~is comprises~~ a polymer selected from polysaccharides, nucleic acids, carbohydrates, proteins, polypeptides, poly(α -hydroxy acids), poly(lactones), poly(amino acids), poly(anhydrides), poly(orthoesters), poly(anhydride-co-imides), poly(orthocarbonates), poly(α -hydroxy alkanooates), poly(dioxanones), poly(phosphoesters), poly(L-lactide) (PLLA), poly(D,L-lactide) (PDLLA), polyglycolide (PGA), poly(lactide-co-glycolide (PLGA), poly(L-lactide-co-D, L-lactide), poly(D,L-lactide-co-trimethylene carbonate), polyhydroxybutyrate (PHB), poly(ϵ -caprolactone), poly(δ -valerolactone), poly(γ -butyrolactone), poly(caprolactone), polyacrylic acid, polycarboxylic acid, poly(allylamine hydrochloride), poly(diallyldimethylammonium chloride), poly(ethyleneimine), polypropylene fumarate, polyvinyl alcohol, polyvinylpyrrolidone, polyethylene, polymethylmethacrylate, carbon fibers, poly(ethylene glycol), poly(ethylene oxide), poly(vinyl alcohol), poly(vinylpyrrolidone), poly(ethyloxazoline), poly(ethylene oxide)-co-poly(propylene oxide) block copolymers, poly(ethylene terephthalate)polyamide, and copolymers thereof.

61. (Withdrawn) The paste of claim 54, wherein said cohesiveness agent is selected from alginic acid, arabic gum, guar gum, xanthan gum, gelatin, chitin, chitosan, chitosan acetate, chitosan lactate, chondroitin sulfate, N,O-carboxymethyl chitosan, a dextran, fibrin glue, glycerol, hyaluronic acid, sodium hyaluronate, a cellulose, a glucosamine, a proteoglycan, a starch, lactic acid, a pluronic, sodium glycerophosphate, collagen, glycogen, a keratin, silk, and mixtures thereof.

62. (Withdrawn) The paste of claim 61, wherein said cellulose is methylcellulose, carboxy methylcellulose, hydroxypropyl methylcellulose, or hydroxyethyl cellulose.

63. (Withdrawn) The paste of claim 61, wherein said dextran is α -cyclodextrin, β -cyclodextrin, γ -cyclodextrin, or sodium dextran sulfate.

64. (Withdrawn) The paste of claim 61, wherein said starch is hydroxyethyl starch or starch soluble.

65. (Withdrawn) The paste of claim 56, wherein said biologically active agent is selected from an antibody, an antibiotic, a polynucleotide, a polypeptide, a protein, an anti-cancer agent, a growth factor, and a vaccine.

66. (Withdrawn) The paste of claim 65 wherein said protein is an osteogenic protein.

67. (Withdrawn) The paste of claim 66, wherein said osteogenic protein is selected from BMP-2, BMP-4, BMP-5, BMP-6, BMP-7, BMP-10, BMP-12, BMP-13, and BMP-14.

68. (Withdrawn – Currently Amended) The paste of claim 65, wherein said anti-cancer agent is selected from alkylating agents, platinum agents, antimetabolites, topoisomerase inhibitors, antitumor antibiotics, antimitotic agents, aromatase inhibitors, thymidylate synthase inhibitors, DNA antagonists, farnesyltransferase inhibitors, pump inhibitors, histone acetyltransferase inhibitors, metalloproteinase inhibitors, ribonucleoside reductase inhibitors, tumor necrosis factor (TNF) TNF alpha agonists, tumor necrosis factor (TNF) TNF alpha antagonists, endothelin A receptor antagonists, retinoic acid receptor agonists, immuno-modulators, hormonal agents, antihormonal agents, photodynamic agents, and tyrosine kinase inhibitors.

69. (Withdrawn – Currently Amended) The paste of claim 54, wherein said effervescent agent is sodium bicarbonate, carbon dioxide, air, nitrogen, helium, oxygen, ~~or~~ and argon.

70. (Withdrawn – Currently Amended) The paste of claim 69, wherein said effervescent agent ~~comprises is present in an amount in the range of~~ about 1 to about 40 wt% of said powder component.

71. (Withdrawn) The paste of claim 38, wherein said paste self-hardens to a PCA calcium phosphate having an overall Ca/P ratio of less than about 1.67.

72. (Withdrawn) The paste of claim 71, wherein said paste self-hardens to a PCA calcium phosphate having an overall Ca/P ratio of less than about 1.5.

73. (Withdrawn) The paste of claim 38, wherein said paste self-hardens to a PCA calcium phosphate having an overall Ca/P ratio in the range of about 1.0 to about 1.67.

74. (Withdrawn) The paste of claim 38, wherein said paste hardens to form a PCA

calcium phosphate having a compressive strength in the range of about 1 MPa to about 20 MPa.

75. (Withdrawn) The paste of claim 74, wherein said paste hardens to form a PCA calcium phosphate having a compressive strength in the range of about 2 MPa to about 10 MPa.

76. (Withdrawn) The paste of claim 38, wherein said paste hardens to form a PCA calcium phosphate having a compressive strength of about 2 MPa.

77. (Withdrawn – Currently Amended) A formable, self-hardening, poorly crystalline apatitic (PCA) calcium phosphate paste suitable for use as a bone implant material comprising:

(a) a powder component, including:

(i) demineralized bone matrix (DBM) particles in an amount in the range of about 40 to about 70 wt%,

(ii) a calcium phosphate powder in an amount in the range of about 25 to about 60 wt%, and

(iii) a biocompatible cohesiveness agent in an amount in the range of about 0.5 to 20 wt%; and

(b) a physiologically acceptable fluid in an amount to produce a cohesive, formable paste, wherein said paste retains its cohesiveness when introduced at an implant site *in vivo* and hardens to form a PCA calcium phosphate having a compressive strength of greater than at least about 1 MPa.

78. (Withdrawn – Currently Amended) A formable, self-hardening, poorly crystalline apatitic (PCA) calcium phosphate paste suitable for use as a bone implant material comprising:

(a) a powder component, ~~comprising~~ including:

(i) demineralized bone matrix (DBM) particles, ~~wherein said demineralized bone~~

matrix particles are present in an amount in the range of between about 40 ± wt% to and about 70 50 wt% of said powder component, and

(ii) a calcium phosphate powder in an amount in the range of about 25 wt% to about 60 wt% of said powder component, wherein said calcium phosphate powder comprises comprised of an amorphous calcium phosphate and a second calcium phosphate having source, wherein said amorphous calcium phosphate and said second calcium phosphate source have an average crystalline domain size of less than about 100nm and wherein said calcium phosphate powder is present in an amount between about 50 wt% and about 99 wt% of said powder component, and

(b) a physiologically acceptable fluid in an amount to produce a coherent, formable paste, wherein said paste retains its cohesiveness when introduced at an implant site *in vivo* and hardens to form a poorly crystalline apatitic (PCA) calcium phosphate having a compressive strength between about 1 MPa and about 20 MPa.

79. (Withdrawn – Currently Amended) The paste of claim 78 further comprising A formable, self-hardening, poorly crystalline apatitic (PCA) calcium phosphate paste suitable for use as a bone implant material comprising:

(a) a powder component, including:

(i) demineralized bone matrix (DBM) particles, wherein said demineralized bone matrix particles are present in an amount between about 1 wt% and about 50 wt% of said powder component;

(ii) a calcium phosphate powder comprised of an amorphous calcium phosphate and a second calcium phosphate source, wherein said amorphous calcium phosphate and said second calcium phosphate source have an average crystalline domain size of less than about 100nm and wherein said calcium phosphate powder is present in an amount between about 50 wt% and about 99 wt% of said powder component, and

(iii) a biocompatible cohesiveness agent, wherein said cohesiveness agent is present in an amount in the range of between about 0.5 ± wt% to and about 20 wt% of said

powder component; and

(b) a physiologically-acceptable fluid in an amount to produce a coherent, formable paste, wherein said paste retains its cohesiveness when introduced at an implant site *in vivo* and hardens to form a poorly crystalline apatitic (PCA) calcium phosphate having a compressive strength between 1 MPa and 20 MPa.

80. (Withdrawn – Currently Amended) A bone implant material comprising a poorly crystalline apatitic (PCA) calcium phosphate, wherein said PCA calcium phosphate is formed by combining:

(a) a powder component comprising, including:

(i) demineralized bone matrix (DBM) particles in an amount in the range of about 40 wt% to about 70 wt% of said powder component.

(ii) a calcium phosphate powder comprising ~~comprised of~~ an amorphous calcium phosphate and a second calcium phosphate source, wherein said second calcium phosphate source is an acidic calcium phosphate, and

(iii) a biocompatible cohesiveness agent; and

(b) a physiologically-acceptable fluid,

wherein said powder component and said liquid combine to produce a paste that hardens to form a PCA calcium phosphate having a compressive strength between about 1 MPa and about 20 MPa.

81. (Cancelled)

82. (Withdrawn – Currently Amended) A method of bone repair comprising introducing the providing a bone implant material of claim 38 into a patient in need thereof at a site requiring bone repair, comprising a poorly crystalline apatitic (PCA) calcium phosphate, wherein said

PCA calcium phosphate is formed by combining:

(a) a powder component, including:

(i) demineralized bone matrix (DBM) particles;

(ii) a calcium phosphate powder comprised of an amorphous calcium phosphate and a second calcium phosphate source, wherein said second calcium phosphate source is an acidic calcium phosphate; and

(iii) a biocompatible cohesiveness agent; and

(b) a physiologically acceptable fluid;

wherein said powder component and said liquid combine to produce a paste that hardens to form a PCA calcium phosphate having wherein, upon hardening, said bone implant material has a compressive strength between about 1 MPa and about 20 MPa.

83. (Cancelled)

84. (New) The osteoinductive powder of claim 1, wherein said paste is capable of hardening to form a PCA calcium phosphate having a compressive strength of between about 1 MPa and 20 MPa.

85. (New) The osteoinductive powder of claim 1, wherein said paste is capable of hardening to form a PCA calcium phosphate having a compressive strength of between about 2 MPa and 10 MPa.

86. (New) The osteoinductive powder of claim 37, wherein said paste is capable of hardening to form a PCA calcium phosphate having a compressive strength of between about 1

MPa and 20 MPa.

87. (New) The osteoinductive powder of claim 37, wherein said paste is capable of hardening to form a PCA calcium phosphate having a compressive strength of between about 2 MPa and 10 MPa.

88. (New) The paste of claim 38, wherein said paste hardens to form a PCA calcium phosphate having a compressive strength of between about 1 MPa and 20 MPa.

89. (New) The paste of claim 38, wherein said paste hardens to form a PCA calcium phosphate having a compressive strength of between about 2 MPa and 10 MPa.

90. (New) The paste of claim 77, wherein said paste hardens to form a PCA calcium phosphate having a compressive strength of between about 1 MPa and 20 MPa.

91. (New) The paste of claim 77, wherein said paste hardens to form a PCA calcium phosphate having a compressive strength of between about 2 MPa and 10 MPa.

92. (New) The paste of claim 78, wherein said paste hardens to form a PCA calcium phosphate having a compressive strength of between about 2 MPa and 10 MPa.

93. (New) The bone implant material of claim 80, wherein said paste hardens to form a PCA calcium phosphate having a compressive strength of between about 2 MPa and 10 MPa.

94. (New) The method of claim 82, wherein, upon hardening, said bone implant material has a compressive strength of between about 2 MPa and 10 MPa.